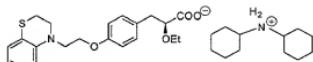


[0052] Mass m/z : 388 (M⁺ + 1), 130 (C₄H₁₁N₅), 113 (C₄H₈N₄).

[0053] Anal:Calcd. : C₂₅H₃₆N₆O₄S, % C 58.12; % H 6.97%, % N 16.3, Found % C 57.95%, % H 6.61, % N 16.25.

Example 3

Dicyclohexylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0054] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (5.0g) and isopropanol (50 ml) were added to 250 ml four necked round bottom flask fitted with a mechanical stirrer and reflux condenser. The reaction was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass.

Dicyclohexylamine (2.33g) in isopropanol (20 ml) was added to the reaction mixture at 55-65°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 75-85°C for 12-14 h and monitored the progress of the reaction by TLC. The reaction mixture was concentrated on rotavapor bath at 45-55°C under reduced pressure to its half volume. The concentrated reaction mixture was cooled to RT and stirred for 2-3 h at room temperature. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure dicyclohexylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as off-white crystalline solid (weighs about 5.1 g, yield : 70 %, m.p. : 110°C, purity by HPLC : 98.99 %).

[0055] IR (KBr) cm⁻¹ : 2932 (C-H aliphatic stretch), 2700-2200 (-NH₃ bands), 1582 (-COO stretch).

[0056] ¹H NMR (200 MHz, DMSO-d₆)δ : 1.0 (t, 3H, CH₃-CH₂-O), 1.2-2.0 (m, 22H, Cyclohexyl), 2.4-3.4 (m, 5H, -S-CH₂, Ar-CH₂, -CH-Ar), 3.45-4.0 (m, 7H, -CH₂-N-CH₂-, CHOEt, CH₂-CH₂-O-), 4.05 (q, 2H, -OCH₂), 6.5 (t, 1H, -CH₂-CH-), 6.7-7.4 (m, 8H, aromatic).

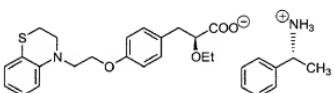
[0057] Mass m/z : 388 (M⁺ + 1) 182 (C₁₂H₂₃N).

[0058] Anal : Calcd. : C₃₃H₄₈N₆O₄S, % C 69.71; % H 8.45%, % N 4.92, Found

% C 69.60%, % H 8.35, % N 4.75.

Example 4

(R)-(+)-Methyl benzylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0059] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (5.0 g) and isopropanol (50 ml) were added to 250 ml four necked round bottom flask fitted with a mechanical stirrer and reflux condenser. The reaction was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. R-(+)-Methyl benzylamine (1.5 g) in isopropanol (20 ml) was added to the reaction mixture of 55-65°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 75-85°C for 12-14 h and monitored the progress of the reaction. The reaction mixture was cooled to 25-35°C and stirred for 2-3 h. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure (R)-(+)-methylbenzylamine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxypropanoic acid as off-white crystalline solid (weighs about 6 g, yield : 91%, m.p. 126-128°C; purity : 98.56 – 99.3 % by HPLC).

[0060] IR (KBr) cm^{-1} : 2983-2856 (-N⁺H stretch), 1637(-COO, Stretch).

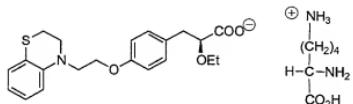
[0061] ¹H NMR (200 MHz, CD₃OD)δ : 1.1 (t, 3H, CH₃-CH₂-O), 1.6 (d, 3H, CH₃-CH-), 2.6-3.4 (m, 5H, -S-CH₂-; Ar-CH₂, -CH-Ar), 3.45-4.0 (m, 7H, -CH₂N-CH₂-; -CH-OEt, CH₂-CH₂-O), 4.05 (q, 2H, -O-CH₂-) 6.5 (t, 1H, CH₂CH₂-CH₂-N-CH₂), 6.7-7.4 (m, 13H, aromatic).

[0062] Mass m/z : 388 (M⁺ + 1), 121(C₈H₁₁N), 105 (C₈H₈)

[0063] Anal : Calcd. : C₂₉H₃₆N₂O₄S, % C 68.50; % H 7.08%, % N 5.51, Found % C 68.38, % H 6.9, % N 5.4.

Example 5

L-Lysine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid



[0064] (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (2.5 g) and isopropanol (25 ml) were added to the 100 ml four necked round bottom flask, fitted with a mechanical stirrer and reflux condenser. The reaction mixture was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. L-Lysine monohydrate (1.0 g) dissolved in water (5 ml) was added to the reaction mixture at 45-55°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 80-90°C for 20-24 hrs and monitored the progress of the reaction. The isopropanol was distilled off along with azeotropic distillation of water using Dean-Stark apparatus. Fresh isopropanol (25 ml) was added to the residual reaction mixture and cooled the mixture initially to room temperature followed by cooling to 0-5°C under stirring for 60-90 min. The precipitated product was filtered, dried at 60°C for 2-3 hours to afford the pure L-lysine salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as off white crystalline, hygroscopic solid (weighs about 2.5 g, yield : 78%, m.p. 142-144°C, purity 97.6 – 99.01% by HPLC).

[0065] IR (KBr) cm^{-1} : 3430-3400 (N-H stretch), 2920 (-C-H aliphatic stretch), 2700 - 2200 (-N⁺H₃ stretch), 1585 (-COO⁻ stretch), 1400 (-COO⁻ stretch).

[0066] ¹H NMR spectrum in DMSO-d₆ + TFA (TMS as internal standard) is in confirmation with the assigned structure.

[0067] Mass m/z : 388 (M⁺ + 1), 164 (C₆H₁₆N₂O₃), 147 (C₆H₁₃NO₃).

[0068] Anal. Calcd for C₂₇H₄₁N₃O₇S; % C : 58.8; % H 7.44%; % N 7.62%, Found % C 58.7; % H 7.28; % N 7.55.